Complete Summary

GUIDELINE TITLE

Recommendations for identification and public health management of persons with chronic hepatitis B virus infection.

BIBLIOGRAPHIC SOURCE(S)

Weinbaum CM, Williams I, Mast EE, Wang SA, Finelli L, Wasley A, Neitzel SM, Ward JW, Centers for Disease Control and Prevention (CDC). Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. MMWR Recomm Rep 2008 Sep 19;57(RR-8):1-20. [145 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chronic hepatitis B

GUIDELINE CATEGORY

Counseling
Diagnosis
Evaluation
Management
Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Hospitals
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To update and expand the multiple previous Centers for Disease Control and Prevention (CDC) guidelines for hepatitis B surface antigen (HBsAg) testing
- To include new recommendations for public health evaluation and management of chronically infected persons and their contacts

TARGET POPULATION

- Persons born in regions of high and intermediate hepatitis B virus (HBV) endemicity
- U.S.-born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity
- Injection-drug users
- Men who have sex with men
- Persons needing immunosuppressive therapy
- Persons with elevated serum alanine aminotransferase/aspartate aminotransferase (ALT/AST) of unknown etiology
- Donors of blood, plasma, organs, tissues, or semen
- Hemodialysis patients
- All pregnant women
- Infants born to hepatitis B surface antigen (HBsAg)-positive mothers
- Household, needle-sharing, or sex contacts of persons known to be HbsAg positive
- Persons who are the sources of blood or body fluids for exposures that might require postexposure prophylaxis
- Human immunodeficiency virus (HIV)-positive persons

INTERVENTIONS AND PRACTICES CONSIDERED

1. Testing for hepatitis B surface antigen (HBsAg)

2. Management of persons tested for chronic hepatitis B virus (HBV) infection
    - Vaccination at the time of testing
    - Reporting of positive results to state or local health department
    - Contact management, including identification, testing, and vaccination of sex partners and household and needle-sharing contacts
    - Patient education on preventing transmission and protecting health
    - Medical management of hepatitis B, including history and physical examination, laboratory testing, treatment, lifelong monitoring, and management of co-infections
    - Development of surveillance registries

MAJOR OUTCOMES CONSIDERED

- Morbidity and mortality
- Incidence of hepatitis B virus (HBV) infection

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

During February 7–8, 2007, the Centers for Disease Control and Prevention (CDC) convened a meeting of researchers, physicians, state and local public health professionals, and other persons in the public and private sectors with expertise in the prevention, care, and treatment of chronic hepatitis B. These consultants reviewed available published and unpublished epidemiologic and treatment data, considered whether to recommend testing specific new populations for hepatitis B virus (HBV) infection, and discussed how best to implement new and existing testing strategies. Topics discussed included 1) the changing epidemiology of chronic HBV infection, 2) health disparities caused by the disproportionate HBV-related morbidity and mortality among persons infected as infants and young children in countries with high levels of HBV endemicity, and 3) the increasing benefits of care and opportunities for prevention for infected persons and their contacts. On the basis of this discussion, CDC determined that reconsideration of current guidelines was warranted. This report summarizes current hepatitis B surface antigen (HBsAg) testing recommendations published previously by CDC, expands CDC recommendations to increase the identification of chronically infected persons in the United States, and defines the components of programs needed to identify HBV-infected persons successfully.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The cost-effectiveness of identifying persons with chronic hepatitis B virus (HBV) infection cannot be calculated because treatment options constantly are increasing the number of years of disease-free life, and the various treatments have diverse associated costs. However, testing for hepatitis B surface antigen (HBsAg) in populations in which prevalence of chronic infection is 2% would cost $750–$3,752 for each chronically infected person identified (range represents $15.01 laboratory cost per test–$75 per screening visit; at higher prevalences, the per-case-identified cost would decrease. This is comparable to the cost of other screening programs. Human immunodeficiency virus (HIV) testing in a population with 1% infection prevalence costs $2,133 ([$1,733–$3,733] per positive identified; $16 per test [$13–$28]). Another study determined that the cost to identify each new case of diabetes mellitus using a two-step glucose-based screening process in three volunteer clinics in Minnesota was $4,064 per case identified. The cost of HBsAg testing in populations with $\geq$2% prevalence is substantially lower than the costs per case identified for certain fetal and newborn screening interventions (e.g., screening for newborn hearing disorders [$16,000 per case identified], metabolic disorders [$68,000 per case], neonatal alloimmune thrombocytopenia [NAIT] caused by anti-HPA-1a [$98,771 per case], or fetal Down syndrome [$690,000 per case]).

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Persons who are most likely to be actively infected with hepatitis B virus (HBV) should be tested for chronic HBV infection. Testing should include a serologic assay for hepatitis B surface antigen (HBsAg) offered as a part of routine care and be accompanied by appropriate counseling and referral for recommended clinical evaluation and care. Laboratories that provide HBsAg testing should use a U.S. Food and Drug Administration (FDA)-licensed or FDA-approved HBsAg test and should perform testing according to the manufacturer's labeling, including testing of initially reactive specimens with a licensed, neutralizing confirmatory test. A confirmed HBsAg-positive result indicates active HBV infection, either acute or chronic; chronic infection is confirmed by the absence of immunoglobulin M (IgM) antibody to hepatitis B core antigen (anti-HBc) or by the persistence of HBsAg or HBV DNA for at least 6 months. All HBsAg-positive persons should be considered infectious.

Recommendations and federal mandates related to routine testing for chronic HBV infection have been summarized (see Table below). To determine susceptibility among persons who are at ongoing risk for infection and recommended for vaccination, total anti-HBc or antibody to HBsAg (anti-HBs) also should be tested at the time of serologic testing for chronic HBV infection. New populations recommended for testing are the following:

- **Persons born in geographic regions with HBsAg prevalence of ≥2%**. All persons born in geographic regions with HBsAg prevalence of ≥2% (e.g., much of Eastern Europe, Asia, Africa, the Middle East, and the Pacific Islands) (see Figure 3 and Table 3 in the original guideline document) and certain indigenous populations from countries with overall low HBV endemicity (<2%) (see Table 3 in the original guideline document) should be tested for chronic HBV infection. This includes immigrants, refugees, asylum seekers, and internationally adopted children born in these regions, regardless of vaccination status in their country of origin. Medical screening of applicants for lawful permanent residency in the United States represents an opportunity for education and voluntary HBsAg testing. Because HBsAg prevalence can vary within these regions, additional knowledge about local HBsAg prevalence can be used to guide decision making regarding testing.
- **Persons with behavioral exposures to HBV**. Men who have sex with men (MSM) and past or current injection-drug users (IDUs) have higher prevalence of chronic HBV infection than the overall U.S. population (see Table 5 in the original guideline document) and should be tested for chronic HBV infection. Both of these populations are recommended for routine hepatitis B vaccination, and HBsAg testing is recommended as a component of prevaccination testing for these adults. The first dose of hepatitis B vaccine

should be administered during the same medical visit with serologic testing. However, HBsAg testing is not a requirement for vaccination, and in settings where testing is not feasible, vaccination of recommended populations should continue.

- **Persons receiving cytotoxic or immunosuppressive therapy**. Persons receiving cytotoxic or immunosuppressive therapy (e.g., chemotherapy for malignant diseases, immunosuppression related to organ transplantation, and immunosuppression for rheumatologic and gastroenterologic disorders) should be tested for serologic markers of HBV infection (i.e., HBsAg, anti-HBc, and anti-HBs). Prophylactic antiviral therapy can prevent reactivation in HBsAg-positive patients.
- **Persons with liver disease of unknown etiology**. All persons with persistently elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels of unknown etiology should be tested for HBsAg as part of the medical evaluation of these abnormal laboratory values.

Table. Populations Recommended or Required for Routine Testing for Chronic Hepatitis B Virus (HBV) Infection

Population	Population-Specific Testing Consideration
Persons born in regions of high and intermediate HBV endemicity (HBsAg[a] prevalence ≥2%)[b]	All persons (including immigrants, refugees, asylum seekers, and internationally adopted children) born in regions with high and intermediate endemicity of HBV infection should be tested for HBsAg, regardless of vaccination status in their country of origin.
U.S.-born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity (≥8%)	If not vaccinated as infants in the United States, these persons should be tested regardless of maternal HBsAg status.
Injection-drug users	• First vaccine dose should be given at the same visit as testing for HBsAg.[c] • Testing for anti-HBc[d] or anti-HBs[e] should be done as well to identify susceptible persons.[f] • Susceptible persons should complete a 3-dose hepatitis B vaccine series to prevent infection from ongoing exposure.
Men who have sex with men	• First vaccine dose should be given at the same visit as testing for HBsAg. • Testing for anti-HBc or anti-HBs should be done as well to identify susceptible persons. • Susceptible persons should complete a 3-dose hepatitis B vaccine series to prevent infection from ongoing exposure.
Persons needing	• Serologic testing should test for all

Population	Population-Specific Testing Consideration
immunosuppressive therapy, including chemotherapy, immunosuppression related to organ transplantation, and immunosuppression for rheumatologic or gastroenterologic disorders	markers of HBV infection (HBsAg, anti-HBc, and anti-HBs). • Because of elevated risk of fulminant hepatitis in chronically infected persons once suppressive therapy is initiated and risk for reactivation in persons with resolved infection, persons who are HBsAg-positive should be treated, and persons who are anti-HBc positive should be monitored closely for signs of liver disease.
Persons with elevated ALT/AST[g] of unknown etiology	Testing for HBsAg should be performed along with other examination and laboratory testing in the context of medical evaluation.
Donors of blood, plasma, organs, tissues, or semen	To prevent transmission to recipients, HBsAg, anti-HBc, and HBV-DNA testing are required.
Hemodialysis patients	• Serologic testing should test for all markers of HBV infection (HBsAg, anti-HBc, and anti-HBs) on admission. • To prevent transmission in dialysis settings, hemodialysis patients should be vaccinated against hepatitis B and revaccinated when serum anti-HBs titer falls below 10 mIU/mL. • HBsAg-positive hemodialysis patients should be cohorted. • Vaccine nonresponders should be tested monthly for HBsAg.
All pregnant women	• Women should be tested for HBsAg during each pregnancy, preferably in the first trimester. • If an HBsAg test result is not available or if the mother was at risk for infection during pregnancy, testing should be performed at the time of admission for delivery. • To prevent perinatal transmission, infants of HBsAg-positive mothers and unknown HBsAg status mothers should receive vaccination and postexposure immunoprophylaxis in accordance with recommendations within 12 hours of delivery.
Infants born to HBsAg-positive	• Testing for HBsAg and anti-HBs should

Population	Population-Specific Testing Consideration
mothers	be performed 1 to 2 mos after completion of at least 3 doses of a licensed hepatitis B vaccine series (i.e., at age 9 to 18 months, generally at the next well-child visit) to assess the effectiveness of postexposure immunoprophylaxis. Testing should not be performed before age 9 months or within 1 month of the most recent vaccine dose. • Maternal and infant medical records should be reviewed to determine whether infant received hepatitis B immune globulin and vaccine in accordance with recommendations.
Household, needle-sharing, or sex contacts of persons known to be HBsAg positive	• First vaccine dose should be administered at the same visit as testing for HBsAg. • Testing for anti-HBc or anti-HBs should be performed as well to identify susceptible persons. • Susceptible persons should complete a 3-dose hepatitis B vaccine series to prevent transmission from ongoing exposure.
Persons who are the sources of blood or body fluids for exposures that might require postexposure prophylaxis (e.g., needlestick, sexual assault)	• Test source person for HBsAg and provide exposed person with postexposure prophylaxis if needed. • High levels of vaccination coverage among health-care workers have led to marked decreases in hepatitis B incidence. Health-care and public safety workers with reasonably anticipated occupational exposures to blood or infectious body fluids should be vaccinated against hepatitis B.
HIV-positive persons	• Test for HBsAg and anti-HBc and/or anti-HBs. • Susceptible persons should be vaccinated against hepatitis B to prevent transmission from ongoing exposure. • HIV infection can accelerate progression of HBV-related liver disease. • Antiretroviral medications used to treat HIV infection also have anti-HBV activity. Medical regimens for HIV management

Population	Population-Specific Testing Consideration
	can be tailored according to patient HBV status.

[a] Hepatitis B surface antigen.
[b] High endemicity = HBsAg prevalence of ≥8%; intermediate endemicity = HBsAg prevalence of 2 to 7%.
[c] Unless an established patient-provider relation can ensure that the patient will return for serologic test results and that vaccination can be initiated at that time if the patient is susceptible.
[d] Antibody to hepatitis B core antigen.
[e] Antibody to HBsAg.
[f] Persons lacking immunity, either vaccine-induced or following resolved infection, to HBV infections.
[g] ALT= alanine aminotransferase; AST = aspartate aminotransferase.

Testing Persons with a History of Vaccination

Because some persons might have been infected with HBV before they received hepatitis B vaccination, HBsAg testing is recommended regardless of vaccination history for the following populations:

- **Persons born in geographic regions with HBV prevalence of ≥2%**. The majority of these persons were born either before full implementation of routine infant hepatitis B vaccination in their countries of origin or during a period when newborn vaccination programs were in the early stages of implementation. Because of the difficulty in verifying the vaccination status of foreign-born persons and the high rate of perinatal and early childhood HBV transmission before implementation of routine infant hepatitis B vaccination programs, HBsAg testing is recommended for all persons born in regions with high or intermediate endemicity of HBV infection even if they were vaccinated in their country of origin
- **U.S.-born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity (≥8%)**. Because of the high efficacy of hepatitis B vaccination, persons with HBsAg-negative mothers who completed the vaccine series as infants in the United States do not need to be tested for HBsAg. However, persons vaccinated through catch-up programs as children or adolescents also should be tested if they were likely to have had HBV exposures before vaccination. Prevalence of chronic HBV infection is high among U.S.-born children who were not vaccinated as infants and whose parents were born in regions with high HBV endemicity.
- **Persons who received hepatitis B vaccination as adolescents or adults after the initiation of risk behaviors**. MSM and IDUs who were potentially exposed to HBV (e.g., through sexual activity or injection-drug use) before vaccination should be tested for HBsAg.

Management of Persons Tested for Chronic HBV Infection

Vaccination at the Time of Testing

Persons to be tested who have been recommended to receive hepatitis B vaccination, including those in settings in which universal vaccination is recommended (i.e., sexually transmitted disease [STD]/HIV testing and treatment

facilities, drug-abuse treatment and prevention settings, health-care settings targeting services to IDUs, health-care settings targeting services to MSM, and correctional facilities) should receive the first dose of vaccine at the same medical visit after blood is drawn for testing unless an established patient-provider relation can ensure that the patient will return for serologic test results and that vaccination can be initiated at that time if the patient is susceptible. In venues where vaccination is recommended and testing is not feasible, vaccination still should be provided for all populations for whom it is recommended.

Public Health Management of HBsAg-Positive Persons

The finding of HBsAg in serum is indicative of chronic HBV infection unless the person has signs or symptoms of acute hepatitis. All HBsAg-positive laboratory results should be reported to the state or local health department, in accordance with state requirements for reporting of acute and chronic HBV infection. Chronic HBV infection can be confirmed by verifying the presence of HBsAg in a serum sample taken at least 6 months after the first test, or by the absence of IgM anti-HBc in the original specimen. Standard case definitions for the classification of reportable cases of HBV infection have been published previously.

Contact Management

Sex partners and household and needle-sharing contacts of HBsAg-positive persons should be identified. Unvaccinated past and present sex partners and household and needle-sharing contacts should be tested for HBsAg and for anti-HBc and/or anti-HBs and should receive the first dose of hepatitis B vaccine as soon as the blood sample for serologic testing has been collected. Susceptible persons should complete the vaccine series using an age-appropriate vaccine dose and schedule. Those who have not been vaccinated fully should complete the vaccine series. Contacts determined to be HBsAg-positive should be referred for medical care.

Health-care providers and public health authorities treating persons with chronic HBV infection should obtain the names of their sex contacts and household members and a history of drug use. Providers then can help to arrange for evaluation and vaccination of contacts, either directly or with assistance from state and local health departments. Contact notification is well-established in public STD programs; these programs have the expertise to reach identified contacts of HBsAg-positive patients and might be able to provide guidance on procedures and best practices, or in programs with sufficient capacity, offer assistance to other providers to reach identified contacts. With sufficient resources, identification of contacts should be accompanied by health counseling and include referral of patients and their contacts for other services when appropriate.

The success of contact management for hepatitis B has varied widely, depending on local resources. One study determined that approximately half of providers caring for patients with chronic HBV infection recommended contact vaccination, and <20% of contacts initiated vaccination. In the national perinatal hepatitis B prevention program, approximately 26% of all persons identified as contacts by HBsAg-positive women were tested and evaluated for vaccination by public health departments. In several state and local programs with targeted efforts for adult

hepatitis B prevention, up to 85% of identified contacts have been evaluated; however, many states and cities have no contact identification programs outside the perinatal hepatitis B prevention program. Given the potential for contact notification to disrupt networks of HBV transmission and reduce disease incidence, health-care providers should encourage patients with HBV infection to notify their sex partners, household members, and injection-drug–sharing contacts and urge them to seek medical evaluation, testing, and vaccination.

Patient Education

Medical providers should advise patients identified as HBsAg positive regarding measures they can take to prevent transmission to others and protect their health or refer patients for counseling if needed. Patient education should be conducted in a culturally sensitive manner in the patient's primary language (both written and oral whenever possible). Ideally bilingual, bicultural, medically trained interpreters should be used when indicated.

- To prevent or reduce the risk for transmission to others, HBsAg-positive persons should be advised to
    - Notify their household, sex, and needle-sharing contacts that they should be tested for markers of HBV infection, vaccinated against hepatitis B, and, if susceptible, complete the hepatitis B vaccine series
    - Use methods (e.g., condoms) to protect nonimmune sex partners from acquiring HBV infection from sexual activity until the sex partners can be vaccinated and their immunity documented (HbsAg-positive persons should be made aware that use of condoms and other prevention methods also might reduce their risks for HIV infection and other STDS)
    - Cover cuts and skin lesions to prevent the spread of infectious secretions or blood
    - Clean blood spills with bleach solution
    - Refrain from donating blood, plasma, tissue, or semen
    - Refrain from sharing household articles (e.g., toothbrushes, razors, or personal injection equipment) that could become contaminated with blood
    - Dispose of blood and body fluids and medical waste properly
- HBsAg-positive pregnant women should be advised of the need for their newborns to receive hepatitis B vaccine and hepatitis B immune globulin beginning at birth and to complete the hepatitis B vaccine series according to the recommended immunization schedule.
- To protect the liver from further harm, HBsAg-positive persons should be advised to
    - Seek health-care services from a provider experienced in the management of hepatitis B
    - Avoid or limit alcohol consumption because of the effects of alcohol on the liver, with referral to care provided for persons needing evaluation or treatment for alcohol abuse
    - Obtain vaccination against hepatitis A (2 doses, 6 to 18 months apart) if chronic liver disease is present
- When seeking medical or dental care, HBsAg-positive persons should be advised to inform those responsible for their care of their HBsAg status so they can be evaluated and their care managed appropriately.

Other counseling messages include the following:

- HBV is not spread by breastfeeding, kissing, hugging, coughing, ingesting food or water, sharing eating utensils or drinking glasses, or casual touching.
- Persons should not be excluded from school, play, child care, work, or other settings on the basis of their HBsAg status, unless they are prone to biting.
- HBV-infected health-care workers should follow published guidelines and applicable state laws and regulations regarding recommended practices to reduce the risk of HBV transmission in the workplace.*
- Involvement with a support group might help patients cope with chronic HBV infection.

*Disagreement exists internationally about best practice for avoiding transmission of HBV from health-care worker to patient.

Medical Management of Chronic Hepatitis B

Because 15% to 25% of persons with chronic HBV infection are at risk for premature death from cirrhosis and liver cancer, persons with chronic HBV infection should be evaluated soon after infection is identified by referral to or in consultation with a physician experienced in the management of chronic liver disease. When assessing chronic HBV infection, the physician must consider the level of HBV replication and the degree of liver injury. Injury is assessed using serial tests of serum aminotransferases (ALT and AST), and, when needed, liver biopsy (histologic activity and fibrosis scores).

Initial evaluation of patients with chronic HBV infection should include a thorough history and physical examination, with special emphasis on risk factors for coinfection with HIV and hepatitis C virus (HCV), alcohol use, and family history of HBV infection and liver cancer. Laboratory testing should assess for indicators of liver disease (complete blood count and liver panel), markers of HBV replication (HBeAg, anti-HBe, HBV DNA), coinfection with HCV, hepatitis D virus (HDV), and HIV, and antibody to hepatitis A virus (HAV) (if local HAV prevalence makes prevaccination testing cost effective). Where testing is available, schistosomiasis (*S. mansoni* or *S. japonicum*) also should be assessed for persons from endemic areas) because schistosomiasis might increase progression to cirrhosis or hepatocellular carcinoma (HCC) in the presence of HBV infection. Persons with chronic HBV infection who are not known to be immune to HAV should receive 2 doses of hepatitis A vaccine 6 to 18 months apart. Baseline alfa fetoprotein assay (AFP) is used to assess for evidence of HCC at initial diagnosis of HBV infection, and ultrasound in patients at risk of HCC (i.e., Asian men aged >40 years, Asian women aged >50 years, persons with cirrhosis, persons with a family history of HCC, Africans aged >20 years, and HBV-infected persons aged >40 years with persistent or intermittent ALT elevation and/or high HBV DNA). Liver biopsy (or, ideally, noninvasive markers) can be used to assess inflammation and fibrosis if initial laboratory assays suggest liver damage, as per published practice guidelines for liver biopsy in chronic HBV infection.

Following an initial evaluation, all patients with chronic HBV infection, even those with normal aminotransferase levels, should receive lifelong monitoring to assess progression of liver disease, development of HCC, need for treatment, and response to treatment. Frequency of monitoring depends on several factors,

including family history, age, and the condition of the patient; monitoring schedules have been recommended by several authorities.

Therapy for hepatitis B is a rapidly changing area of clinical practice. Seven therapies have been approved by FDA for the treatment of chronic HBV infection: interferon alfa-2b, peginterferon alfa-2a, lamivudine, adefovir dipivoxil, entecavir, telbivudine, and tenofovir disoproxil fumarate. In addition, at least two other FDA-approved oral antiviral medications for HIV (clevudine and emtricitabine) are undergoing phase-3 trials for HBV treatment and might be approved soon for chronic hepatitis B. Treatment decisions are made on the basis of HBeAg status, HBV DNA viral load, ALT, stage of liver disease, age of patient, and other factors.

Coinfection with HIV complicates the management of patients with chronic hepatitis B. When selecting antiretrovirals for HIV treatment, the provider must consider the patient's HBsAg status to avoid liver-associated complications and development of antiviral resistance. Management of these patients has been described elsewhere.

Serologic endpoints of antiviral therapy are loss of HBeAg, HBeAg seroconversion in persons initially HBeAg positive, suppression of HBV DNA to undetectable levels by sensitive PCR-based assays in patients who are HBeAg-negative and anti-HBe positive, and loss of HBsAg. Optimal duration of therapy has not been established. For HBeAg-positive patients, treatment should be continued for at least 6 months after loss of HBeAg and appearance of anti-HBe; for HBeAg-negative/anti-HBe-positive patients, relapse rates are 80% to 90% if treatment is stopped in 1 to 2 years. Viral resistance to lamivudine occurs in up to 70% of persons during the first 5 years of treatment. Lower rates of resistance among treatment-naïve patients have been observed with adefovir (30% in 5 years), entecavir (<1% at 4 years), and telbivudine (2.3% to 5% in 1 year) but more resistance might occur with longer usage or among patients who developed resistance previously to lamivudine. Although combination therapy has not demonstrated a higher rate of response than that using the most potent antiviral medication in the regimen, more studies are needed using combinations of different classes of different medications active against HBV to determine if combination therapy will reduce the rate of the development of resistance.

Development of Surveillance Registries of Persons with Chronic HBV Infection

Information systems, or registries, of persons with chronic HBV infection can facilitate the notification, counseling, and medical management of persons with chronic HBV infection. These registries can be used to distinguish newly reported cases of infection from previously identified cases, facilitate and track case follow-up, enable communication with case contacts and medical providers, and provide local, state, and national estimates of the proportion of persons with chronic HBV infection who have been identified. Public health agencies use registries for patient case management as part of disease control programs for HIV and tuberculosis; for tracking cancers; and for identifying disease trends, treatment successes, and outcomes. Chronic HBV registries can similarly be used as a tool for public health program and clinical management. Widespread registry use for chronic HBV infection will be facilitated by the development of better algorithms for deduplication (i.e., methods to ensure that each infected person is represented

only once), routine electronic reporting of laboratory results, and improved communication with laboratories.

A tiered approach to establishing a registry might allow programs to increase incrementally the number of data elements collected and the expected extent of follow-up as resources become available. The specific data elements to be included will depend upon the objectives of the registry and the feasibility of collecting that information. At a minimum, sufficient information should be collected to distinguish newly identified persons from those reported previously, including demographic characteristics and serologic test results. If an IgM anti-HBc result is not reported, information about the clinical characteristics of the patient (e.g., presence of symptoms consistent with acute viral hepatitis, date of symptom onset, and results of liver enzyme testing) and the reason for testing can help ensure that the registry includes only persons with chronic infection and excludes those with acute disease. Including data elements on ethnicity and/or country of birth can assist in targeting interventions, and information about contacts identified and managed and medical referrals made can be used to review program needs.

Collaboration between the registry and the perinatal hepatitis B prevention program is important to ensure that the registry captures data on women and infants with chronic infection identified through the perinatal hepatitis B prevention program. Conversely, the perinatal hepatitis B prevention program can use registry data to identify outcomes for infants born to infected women who might have been lost to follow-up. Periodic cross-matches with local cancer registry and death certificate data can allow a program to estimate the contribution of chronic HBV infection to cancer and death rates. Guidelines that clarify how and when data with or without personal identifiers are transmitted and used should be developed to facilitate the protection of confidential data.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- With recent advances in hepatitis B treatment and detection of liver cancer, identification of a hepatitis B virus (HBV)-infected person permits the implementation of important interventions to reduce morbidity and mortality.
- Identification of infected persons also allows for primary prevention of ongoing HBV transmission by enabling persons with chronic infection to adopt behaviors that reduce the risk of transmission to others and by permitting

identification of close contacts who require testing and subsequent vaccination (if identified as susceptible) or medical management (if identified as having chronic HBV infection).
- Appropriate hepatitis B surface antigen (HBsAg) testing and counseling also help prevent health-care--associated transmission in dialysis settings by allowing for cohorting of infected patients.

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This report does not include any discussion of the unlabeled use of a product or a product under investigational use.
- Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation of Testing Recommendations

Health departments provide clinical services in a variety of settings serving persons recommended for hepatitis B surface antigen (HBsAg) testing, including many foreign-born persons, men who have sex with men (MSM), and injection-drug users (IDUs). Ideally, HBsAg testing should be available in venues such as homeless shelters, jails, sexually transmitted disease (STD) treatment clinics, and refugee clinics. Because of the increased representation of IDUs and former IDUs in homeless shelters (58% drug users), substance abuse treatment programs (13%–50% IDUs), and correctional facilities (25% IDUs) and the over-representation of IDUs and MSM in STD clinics (6% IDUs and 10% MSM), prevalence of chronic HBV infection is likely to be higher in these settings. However, few states have resources to implement HBsAg testing programs in these settings and rely instead on limited community programs for needed public health and medical management.

In 2008, the Centers for Disease Control and Prevention (CDC) supported adult viral hepatitis prevention coordinators (AVHPCs) in 49 states, the District of Columbia, and five cities (Los Angeles, Chicago, New York City, Philadelphia, and Houston) who assist in integrating hepatitis A and hepatitis B vaccination, hepatitis B and hepatitis C testing, and prevention services among MSM, IDUs, and at-risk heterosexuals treated in STD clinics, HIV testing programs, substance abuse treatment centers, correctional facilities, and other venues. AVHPCs can promote the implementation of hepatitis B screening for MSM and IDUs. Testing in refugee and immigrant health centers and other health-care venues is needed to

reach U.S. residents born in regions with HBsAg prevalence of $\geq$2%; AVHPCs also can collaborate within these settings to ensure that persons from HBV-endemic regions are tested for HBsAg.

CDC's perinatal hepatitis B prevention program provides case management for HBsAg-positive mothers and their infants, including educating mothers and providers about appropriate follow-up and medical management. This program currently identifies 12,000 to 13,000 HBsAg-positive pregnant women each year. Although perinatal prevention programs provide follow-up for infants born to HBV infected women, the majority of states and local perinatal prevention programs lack staff to offer care referrals for HBV infected pregnant women.

Multiple health-care providers play a role in identifying persons with chronic HBV infection and should seek ways to implement testing for chronic HBV in clinical settings: primary care, obstetrician, and other physician offices, refugee clinics, tuberculosis (TB) clinics, substance abuse treatment programs, dialysis clinics, employee health clinics, university health clinics, and other venues. Medical compliance with testing recommendations already is high for certain populations, particularly among those who typically receive care in hospitals or other health-care settings in which HBsAg testing is routine. For example, 99% of pregnant women deliver their infants in hospitals and 89% to 96% of them are tested for HBV infection, and susceptible dialysis patients are tested monthly for HBsAg. However, compliance with testing recommendations is lower in other settings. One study indicated that testing was performed for 30% to 50% of persons born in regions with high HBsAg prevalence who were seen in public primary care clinics. Even in settings in which persons are tested routinely for HBsAg, more efforts are needed to educate, evaluate, and refer clients for appropriate medical follow-up. CDC supports education and training grants that help educate providers to screen patients at risk for chronic hepatitis B. Prevention research is needed to guide the delivery of hepatitis B screening in diverse clinical and community settings.

In addition, community outreach and education, conducted through developing partnerships between health departments and community organizations, is needed to encourage community members to seek HBsAg testing. These partnerships might be particularly important to overcome social and cultural barriers to testing and care among members of racial and ethnic minority populations who are unfamiliar with the U.S. health-care system. Advisory groups of community representatives, providers who treat patients for chronic hepatitis B, providers whose patient populations represent populations with high prevalence, and professional medical organizations can guide health departments in developing communications and prioritizing hepatitis B screening efforts.

The lack of sufficient resources for management of infected persons can be a barrier to implementation of screening programs. All persons with HBV infection, including those who lack insurance and resources, will need ongoing medical management and possibly therapy. This demand for care will increase as screening increases, and additional providers will be needed with expertise in the rapidly evolving field of hepatitis B monitoring and treatment.

IMPLEMENTATION TOOLS

Foreign Language Translations
Patient Resources
Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Weinbaum CM, Williams I, Mast EE, Wang SA, Finelli L, Wasley A, Neitzel SM, Ward JW, Centers for Disease Control and Prevention (CDC). Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. MMWR Recomm Rep 2008 Sep 19;57(RR-8):1-20. [145 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Sep 19

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Cindy M. Weinbaum, MD; Ian Williams, PhD; Eric E. Mast, MD; Susan A. Wang, MD; Lyn Finelli; Annemarie Wasley, ScD; Stephanie M. Neitzel; John W. Ward, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The Centers for Disease Control and Prevention (CDC), their planners, and their content experts wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers, or commercial services, or commercial supporters.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site:

- HTML Format
- Portable Document Format (PDF)

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. Continuing education activity. Available from the Centers for Disease Control and Prevention (CDC) Web site.

PATIENT RESOURCES

Patient education resources concerning hepatitis B virus infection are available (in various languages) on the Centers for Disease Control Prevention (CDC) Web site.

NGC STATUS

This NGC summary was completed by ECRI Institute on October 10, 2008.

COPYRIGHT STATEMENT

No copyright restrictions apply.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 11/3/2008